

PATENT COOPERATION TREATY

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From the INTERNATIONAL SEARCHING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT AND
THE WRITTEN OPINION OF THE INTERNATIONAL
SEARCHING AUTHORITY, OR THE DECLARATION

To:	Reference	Country
NOVO NORDISK A/S		
Corporate Patents		
Novo Allé	Agent	Short title
DK-2880 Bagsvaerd	22. JUL. 2004	
DENMARK	Action	Term

(PCT Rule 44.1)

Date of mailing
(day/month/year)

22/07/2004

Applicant's or agent's file reference

6624.204-wo

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/DK2004/000163

International filing date
(day/month/year)

18/03/2004

Applicant

NOVO NORDISK A/S

1. ☒ The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes
1211 Geneva 20, Switzerland, Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.
3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

- ☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- ☐ no decision has been made yet on the protest: the applicant will be notified as soon as a decision is made

4. Reminders

Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices.

In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Geertruida Groeneveld-Van der Spek

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged,
- (ii) the claim is cancelled,
- (iii) the claim is new,
- (iv) the claim replaces one or more claims as filed,
- (v) the claim is the result of the division of a claim as filed

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged, claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled, new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled, claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)".

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 6624 . 204 -wo	FOR FURTHER ACTION see Form PCT/ISA/220 as well as, where applicable, item 5 below.	
International application No. PCT/DK2004/000183	International filing date (day/month/year) 18/03/2004	(Earliest) Priority Date (day/month/year) 18/03/2003
Applicant NOVO NORDISK A/S		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 6 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. ☐ **Certain claims were found unsearchable** (See Box II).

3. ☐ **Unity of invention is lacking** (see Box III).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

METHOD FOR THE PRODUCTION OF GLA-RESIDUE CONTAINING SERINE PROTEASES

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority

6. With regards to the drawings,

- a. the figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ as selected by this Authority, because the applicant failed to suggest a figure.

☐ as selected by this Authority, because this figure better characterizes the invention.

- b. ☒ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK2004/000183

A. CLASSIFICATION OF SUBJECT MATTER
 IPC 7 C12N9/64 A61K38/48

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
X	<p>KLAUSEN N K ET AL: "Analysis of the glycoforms of human recombinant factor VIIa by capillary electrophoresis and high-performance liquid chromatography" JOURNAL OF CHROMATOGRAPHY A, ELSEVIER SCIENCE, NL, vol. 718, no. 1, 1 December 1995 (1995-12-01), pages 195-202, XP004038516 ISSN: 0021-9673 page 197 - page 198; figure 1</p> <p>----- -/--</p>	1-83

☒ Further documents are listed in the continuation of box C

☒ Patent family members are listed in annex

* Special categories of cited documents

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

Z document member of the same patent family

Date of the actual completion of the international search

30 June 2004

Date of mailing of the international search report

22/07/2004

Name and mailing address of the ISA

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Authorized officer

Schmidt, Harald

INTERNATIONAL SEARCH REPORT

International Application No

PCT/DK2004/000183

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document with indication, where appropriate, of the relevant passages	Relevant to claim No
X	TOMOKIYO K ET AL.: "Large-scale production and properties of human plasma-derived activated Factor VII concentrate" VOX SANGUINIS, vol. 84, no. 1, January 2003 (2003-01), pages 54-64, XP002286502 page 56 - page 57 -----	44-83
X	EP 0 770 625 A (BEHRINGWERKE AG) 2 May 1997 (1997-05-02) column 1, line 41 - column 3, line 54; claim 3 -----	1-83
X	US 5 700 914 A (JORGENSEN TONY ET AL) 23 December 1997 (1997-12-23) cited in the application column 1, line 31 - line 36; examples 1-4 -----	1-83
X	EP 0 547 932 A (AQUITAINE DEV TRANSF SANGUINE) 23 June 1993 (1993-06-23) claims 1,8,9; example 1 -----	24-83
X	EP 0 765 669 A (IMMUNO AG) 2 April 1997 (1997-04-02) examples 2,3,5 -----	24-83
P,O, X	KRARUP JC & HANSEN TB: "Studies on coagulation factor VIIa autoproteolysis and formation of degradation products" ABSTRACTS OF PAPERS AMERICAN CHEMICAL SOCIETY 2003, vol. 225, no. 1-2, 23 March 2003 (2003-03-23), page BIOT333, XP008032287 abstract -----	1-83
P,X	WO 03/092731 A (NOVO NORDISK AS) 13 November 2003 (2003-11-13) page 12, line 3 - page 13, line 2; claims 5,31,35,38 -----	44-83

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-43

methods for production of a purified GLA-residue containing serine protease

2. claims: 44-83

method for stabilizing a GLA-residue containing serine protease and composition comprising a GLA-residue containing serine protease

INTERNATIONAL SEARCH REPORT

International application No.
PCT/DK2004/000183

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos. :
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims, it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/DK2004/000183

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0770625	A	02-05-1997	DE 19538715 A1	30-04-1997
			AT 221085 T	15-08-2002
			AU 706057 B2	10-06-1999
			AU 7022696 A	24-04-1997
			CA 2188093 A1	19-04-1997
			DE 59609474 D1	29-08-2002
			EP 0770625 A2	02-05-1997
			ES 2180680 T3	16-02-2003
			JP 9165397 A	24-06-1997
			US 2001007901 A1	12-07-2001
US 5700914	A	23-12-1997	AU 677309 B2	17-04-1997
			AU 6423994 A	24-10-1994
			CA 2159313 A1	13-10-1994
			CN 1121723 A ,B	01-05-1996
			CZ 9502533 A3	17-01-1996
			WO 9422905 A1	13-10-1994
			EP 0691984 A1	17-01-1996
			FI 954649 A	29-09-1995
			HU 72712 A2	28-05-1996
			JP 8508264 T	03-09-1996
			NO 953883 A	28-11-1995
			PL 310887 A1	08-01-1996
			ZA 9401956 A	30-09-1994
EP 0547932	A	23-06-1993	FR 2684999 A1	18-06-1993
			AT 142255 T	15-09-1996
			DE 69213421 D1	10-10-1996
			DE 69213421 T2	03-04-1997
			DE 547932 T1	03-02-1994
			DK 547932 T3	10-02-1997
			EP 0547932 A1	23-06-1993
			ES 2056782 T1	16-10-1994
			GR 93300094 T1	30-09-1993
			GR 3021875 T3	31-03-1997
			JP 2533050 B2	11-09-1996
			JP 5345799 A	27-12-1993
			US 5344918 A	06-09-1994
EP 0765669	A	02-04-1997	DE 19531637 A1	06-03-1997
			CA 2184226 A1	01-03-1997
			EP 0765669 A1	02-04-1997
			JP 9110715 A	28-04-1997
			NO 963568 A	03-03-1997
			US 5891843 A	06-04-1999
			US 6013620 A	11-01-2000
WO 03092731	A	13-11-2003	WO 03092731 A1	13-11-2003
			US 2004009918 A1	15-01-2004

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To.

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No
PCT/DK2004/000183

International filing date (day/month/year)
18.03.2004

Priority date (day/month/year)
18.03.2003

International Patent Classification (IPC) or both national classification and IPC
C12N9/64, A61K38/48

Applicant
NOVO NORDISK AS

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis 1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/DK2004/000183

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b))
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ in written format
 - ☐ in computer readable form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in computer readable form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/DK2004/000183

Box No. II Priority

1. ☒ The following document has not been furnished:
- ☒ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).
 - ☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).
- Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date
3. Additional observations, if necessary:

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-83
Inventive step (IS)	Yes: Claims	
	No: Claims	1-83
Industrial applicability (IA)	Yes: Claims	1-83
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)
- and / or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

D1: Klausen NK & Kornfelt T (1995) Journal of Chromatography A, 718:195-202

D2: Tomokiyo K et al. (2003) Vox Sanguinis 84: 54-64

D3: EP 0 770 625

D4: US 5 700 914

D5: EP 0 547 932

D6: EP 0 765 669

Novelty

The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of independent claims 1,24,44 and 64 is not new in the sense of Article 33(2) PCT.

The document D1 discloses (the references in parentheses applying to this document) a method for purification of recombinant factor VIIa wherein said GLA-residue containing serine protease is purified using capillary electrophoresis at pH 4.8 or, alternatively, at pH 9.0.

Further disclosed is a preparation of factor VIIa in a solution with a pH of 4.8 or 9.0 (see page 197, right-hand column to page 198, left-hand column, and figure 1).

Therefore, subject-matter of independent claims 1,24,44 and 64 does not meet the requirements of Article 33(2) PCT.

The document D2 discloses a preparation of human plasma-derived factor VIIa in a buffer having pH 6.9 (see page 57, left-hand column).

Therefore, subject-matter of independent claims 44 and 64 does not meet the requirements of Article 33(2) PCT.

The document D3 discloses a process for purification of recombinant factor VII/VIIa, wherein said proteins are eluted at pH 6.5 from a Sepharose column. Further disclosed is a preparation of factor VIIa in a solution with a pH of 6.5 (see Example).

Therefore, subject-matter of independent claims 1,24,44 and 64 does not meet the requirements of Article 33(2) PCT.

The document D4 discloses a process for purification of recombinant factor VII/VIIa, wherein said proteins are eluted at pH 8.6 from a Q-Sepharose column. Further disclosed is a preparation of factor VIIa in a solution with a pH of 8.6 (see Examples 1 to 4).

Therefore, subject-matter of independent claims 1,24,44 and 64 does not meet the requirements of Article 33(2) PCT.

The document D5 discloses a process for purification of human plasma-derived factor VII/VIIa, wherein said proteins are eluted at pH 6 from a Q-Sepharose column. It is also mentioned that the Sepharose column is equilibrated using a buffer having pH 6. Further disclosed is a preparation of factor VIIa in a solution with a pH of 6 (see Example 1 and claims 8 and 9).

Therefore, subject-matter of independent claims 24,44 and 64 does not meet the requirements of Article 33(2) PCT.

The document D6 discloses a process for purification of human plasma-derived factor VII/VIIa, wherein said proteins are eluted at pH 8.6 from a Q-Sepharose column. Further disclosed is a preparation of factor VIIa in a solution with a pH of 8.6 (see Examples 2,3 and 5).

Therefore, subject-matter of independent claims 24,44 and 64 does not meet the requirements of Article 33(2) PCT.

Dependent claims 1 to 23,25-43,45-63 and 65-83 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, see documents D1 to D6 and the corresponding passages cited in the search report.

Industrial applicability

Subject-matter of claims 1 to 83 meets the requirements of Article 33(4) PCT.

Re Item VI

Certain documents cited

Certain published documents

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/092731	13/11/2003	02/05/2003	03/05/2002

Non-written disclosures

Kind of non-written disclosure	Date of non-written disclosure (day/month/year)	Date of written disclosure referring to non-written disclosure (day/month/year)
meeting abstract (Krarup & Hansen)	23/03/2003 - 27/03/2003	

Re Item VIII

Certain observations on the international application

It is unclear in the sense of Article 6 PCT what is meant with a free calcium ion concentration lower than 0.00 (see claims 5,28,48,68).

Furthermore, a concentration unit should be indicated in said claims in order to comply with Article 6 PCT.

The relative term "about" used in claims 12, 14,35,37,55,57,75 and 77 has no well-recognised meaning and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matter of said claims unclear, Article 6 PCT.

Although claims 1 and 24 have been drafted as separate independent claims, they appear to relate effectively to the same subject-matter and to differ from each other only with regard to the definition of the subject-matter for which protection is sought. The aforementioned claims therefore lack conciseness and as such do not meet the requirements of Article 6 PCT.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No

PCT/DK2004/000183

It is unclear in the sense of Article 6 PCT which divalent cation is meant with "Uo²⁺"
(see claims 7,30,50 and 70).